Generic Pharmaceutical Association

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Dockets Management Branch
Food and Drug Administration
Room 1061, HFA-305
5630 Fishers Lane
Rockville, MD 20852

RE: Docket No. 2003N-0341
Requirements for Submission of In Vivo Bioequivalence Data; Proposed Rule

Comments of the Generic Pharmaceutical Association

Dear Sir or Madam:

The Generic Pharmaceutical Association (GPhA) appreciates the opportunity to comment on the above referenced Proposed Rule. GPhA represents 98% of generic drug manufacturers whose drugs are dispensed for over half of all prescriptions filled in the United States, but represent less than 10% of all drug expenditures. GPhA is the united voice of the generic drug industry and is committed to patient health and safety, and strongly supports any measures that will improve our health care system.

The proposed rule calls for the extension of current submission requirements to include not only submission of complete reports of bioequivalence (BE) studies upon which an application depends for approval, but also summary reports for all others, including nonpassing studies, conducted on the same drug product formulation as the one intended to be marketed.

GPhA Supports Proposed Rule

GPhA supports the proposed rule and agrees that access to the information sought in the proposed rule may be a valuable asset to FDA and provide knowledge for its science mission. GPhA member companies continue to bring safe and effective medicines to the public, and acknowledge the high level of the scientific standards utilized by FDA to review and approve generic drugs. We commend FDA for specifically stating in the proposed rule that:

> "The agency is not aware of any adverse public health consequences associated with products for which studies were not submitted. Moreover, the agency is not aware of any information regarding any generic product currently on the market that would suggest that the product is not bioequivalent to a reference listed drug to which it has been designated as therapeutically equivalent."

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Clear Regulatory Implementation Needed

While GPhA supports the concept of providing the requested information to FDA, careful implementation of the rule will be critical to prevent the application process from becoming unnecessarily cumbersome for both the Agency and industry and slow the availability of affordable medicines to patients. It has been stated publicly on various occasions by Office of Generic Drugs (OGD) staff that BE review, and, response to controlled correspondence by Division of Bioequivalence in OGD are two areas where efforts to reduce review times continue to need attention. The proposed rule calls for review by FDA staff of all studies for all formulations tested that fit the criteria of "sameness" (as defined in the proposed rule) in all applications/amendments/supplements, determination if further information is required from the applicant for any summary reports of studies not relied on for approval, and then evaluation of that forwarded information, through an iterative process. There will need to be some consideration given to providing a timely scientific and practical resolution to such cases where the iterative process becomes protracted such as when there is a difference of scientific opinion between the Agency and applicant.

The proposed rule also provides for inspection of facilities where the BE studies were conducted. Indeed some of these can be foreign entities. Will FDA have sufficient resources to inspect such facilities in a timely manner?

Any new regulations emanating from the proposed rule need to address the review and inspection resource constraints faced by FDA. This is absolutely necessary to ensure that FDA remains committed to Commissioner McClellan's "Project First Review Cycle" that the generic industry and FDA have been working on together so well to reduce ANDA review times. FDA states in the proposed rule that it estimates a 10% increase in the number of biostudies submitted to the agency as parts of original applications, amendments, or supplements. An informal survey of our member companies points to a larger increase based on the impact of statistical design requirements of such studies.

FDA-Industry Dialog Crucial for Successful Implementation

GPhA appreciates the opportunity to comment on the proposed rule and supports it in concept. Since its success is in accomplishing the goal of helping FDA with BE determinations while still maintaining an unnecessarily encumbered approval process to ensure expeditious availability of affordable medicine to the public, GPhA strongly encourages FDA to be especially cognizant of the related science and practical issues such that the best regulatory policy emanates from the proposed rule. We look forward to working collaboratively with FDA to develop the best way to implement the proposed rule.

If you have any questions or wish to contact GPhA to discuss this matter, please contact Steve Bende, Ph.D. at 703-647-2487/steve.bende@gphaonline.org or Gordon Johnston 703-647-2496/Gordon@gphaonline.org.

Thank You,

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